REMARKS

Claims 41, 42, 44-46, 48-50, 56, 57, 62, 63, 65, 66, and 68-73 are pending in this application. Claims 41, 42, 44-46, 48-50, 56, 57, 62, 63, 65, 66, and 68-73 were rejected under 35 U.S.C. § 112, first paragraph. Claims 41, 42, 44-46, 48-50, 65, 66, 68, and 69 were rejected under 35 U.S.C. § 112, second paragraph. Claims 41, 42, 44-46, 48, 49, 65, and 68-71 were rejected under 35 U.S.C. § 103(a).

By this amendment, claims 41, 42, 44-46, 48-50, 65, 66, 68 and 69 have been canceled without prejudice or disclaimer of any previously claimed subject matter. The cancellations are made solely to promote prosecution without prejudice or disclaimer of any previously claimed subject matter. With respect to all amendments and canceled claims, Applicants have not dedicated or abandoned any unclaimed subject matter and moreover have not acquiesced to any rejections and/or objections made by the Patent Office. Applicants expressly reserve the right to pursue prosecution of any presently excluded subject matter or claim embodiments in one or more future continuation and/or divisional application(s).

Applicants have carefully considered the points raised in the Office Action and believe that the Examiner's concerns have been addressed as described herein, thereby placing this case into condition for allowance.

Rejections under 35 U.S.C. §112, first paragraph

Claims 41, 42, 44-46, 48-50, 56, 57, 62, 63, 65, 66, and 68-73 were rejected under 35 U.S.C. §112, first paragraph, for allegedly not enabling any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with the claims. Applicants respectfully traverse this rejection.

Although Applicants believe that the specification provides sufficient guidance for one skilled in the art to make and use the invention of claims 41, 42, 44-46, 48-50, 65, 66, 68 and 69, Applicants have canceled these claims solely to facilitate disposition of the present case. Thus, this rejection of these claims is moot.

Claims 56, 57, 62, 63 and 70-73 are directed to a pharmaceutical composition, a compartmentalized kit and an article of manufacture comprising retinal pigment epithelial (RPE) cells and insulin-producing β cells. Applicants respectfully submit that claims 56, 57, 62, 63 and 71-73 are enabled by the specification, i.e., the specification teaches how to make and use the claimed composition, kit and article of manufacture.

Applicants respectfully submit that the standard for determining an enabling disclosure is not limited to what is described in a particular example of the specification. In fact, the specification need not contain an example if the invention is otherwise disclosed in such manner that one skilled in the art will be able to practice it without an undue amount of experimentation. *In re Borkowski, 422 F.2d 904, 908, 164 USPQ 642, 645 (CCPA 1970)*; M.P.E.P. § 2164.02. The state of the art existing at the filing date of the application is used to determine whether a particular disclosure is enabling as of the filing date. *Chiron Corp. v. Genentech Inc.*, 363 F.3d 1247, 1254, 70 USPQ2d 1321, 1325-26 (Fed. Cir. 2004). The specification need not disclose what is well-known to those skilled in the art and preferably omits that which is well-known to those skilled and already available to the public. *In re Buchner*, 929 F.2d 660, 661, 18 USPQ2d 1331, 1332 (Fed.Cir. 1991); M.P.E.P. §2164.05(a).

In support of this rejection, the Examiner states that the "only disclosed purpose for products comprising RPE and insulin-producing β cells ... is for treating disease." Office Action, page 4. The Examiner maintains the position that "[w]hile Selawry taught using Sertoli cells to deliver β-cells secreting insulin, the specification does not provide adequate correlation between Sertoli cells and RPE such that similar results could be obtained." Office Action, page 7.

Applicants respectfully submit that one skilled in the art does not require a direct comparison of RPE cells to Sertoli cells to enable the claimed invention. Given the state of the art, the specification provides the skilled artisan sufficient guidance to enable the claimed compositions.

Citing Griffith,[1] the specification teaches that the "FasL protein is believed to be particularly important for the prolonged survival of grafted tissue and is believed to act through activation of apoptosis in Fas+, antigen activated T cells of the recipient." Specification, page 2, lines 12-15. Also, Lau describes a study which "investigated whether provision of the FasL signal by transfected syngeneic myoblasts within the local environment of an islet allograft can deliver a death signal to infiltrating allo-activated T cells that express Fas and thereby protect the islet allograft from rejection."[2] Thus, induction of apoptosis in activated T cells in the locale of an allograft was known in the art as a mechanism to prolong survival of the allograft.

Lau demonstrates that cotransplantation of myoblasts engineered to express FasL protect allogeneic islet grafts from immune rejection and result in normoglycemia in mice with diabetes. Lau demonstrates prolonged allogeneic islet graft survival only with cotransplantation of myoblasts expressing FasL and not with control cells, indicating FasL expression is sufficient to prolong survival. The prolonged survival effect was observed over a 200-fold range in the number of cotransplanted FasL-expressing myoblasts. Blood glucose levels of the recipients stabilize at normoglycemic values within the first 10 days after transplantation but revert to pretransplant hyperglycemic values within 48 hours of removing the transplanted cells.[3]

Thus, it was known in the art at the time the application was filed that cotransplantation of FasL-expressing Sertoli cells and genetically engineered myoblasts with insulin secreting β cells results in normoglycemia in diabetic animals.

The specification demonstrates that RPE cells secrete substantial amounts of biologically active FasL sufficient to induce apoptosis in fetal thymocytes, pre-T cells which exist in a high activation state.[4] Given the teaching that RPE cells secrete biologically active FasL in easily measurable amounts, Applicants submit that the number of RPE cells needed to prolong survival time of insulin-producing β cells can be determined by the skilled artisan without undue

[1] Griffith et al., 1995, *Science* 270:1189-1192, "Griffith"; of record.
[2] Lau et al., 1996, *Science* 273:109-112, "Lau"; submitted herewith. See, page 109.
[3] See, for example, Lau, page 111, Table 1 and Fig.3.
[4] See, for example, specification page 16, lines 18-25, and pages 23-28.

experimentation. The specification provides guidelines for the number of RPE cells for administration and for ways of determining immune rejection, or cell survival, of the insulin-producing β cells.[5] Isolation and implantation of insulin-producing β cells was well known in the art at the time of filing,[6] and pharmaceutical reagents and containers for such compositions are described in the specification and also well known in the art.

Thus, the pending claims are in compliance with the enablement requirements. Applicants submit that a *prima facie* case of non-enablement has not been established and that the specification provides sufficient guidance for one skilled in the art to make and use the invention as claimed.

Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejections under 35 U.S.C. § 112, first paragraph.

Rejection under 35 U.S.C. §112, second paragraph

Claims 41, 42, 44-46, 48-50, 65, 66, 68, and 69 were rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. Applicants respectfully traverse this rejection for reasons already of record.

Although Applicants believe that the claims are sufficiently definite when considered in view of the specification and the understanding of those of skill in the art, Applicants have canceled these claims solely to facilitate disposition of the present case.

Thus, this rejection of these claims is moot. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, second paragraph.

[5] See, for example, specification page 15, lines 18-30.
[6] See, for example, Sigalla (1997), Weber (1997), Selawry (U.S. Pat. No. 5,725,854), of record.

Rejection under 35 U.S.C. §103

Claims 41, 42, 44-46, 48, 49, 65, and 68-71 were rejected under 35 U.S.C. §103 as allegedly unpatentable over Cherksey (U.S. Patent No. 5,618,531) as supported by Jorgensen et al. (1997, *Invest. Ophthalmology and Visual Sci.*, 38(4), p. S186, abstract 924; "Jorgensen"). Applicants respectfully traverse this rejection.

Although Applicants believe that claims 41, 42, 44-46, 48, 49, 65, 68, and 69 are not obvious in view of the cited references for reasons of record, Applicants have canceled these claims solely to facilitate disposition of the present case. Thus, this rejection of these claims is moot.

Claims 70 and 71 are directed to a pharmaceutical compositions comprising RPE cells, insulin-producing β cells and a pharmaceutically acceptable carrier. In claim 70, the RPE cells are attached to a matrix and in claim 71, the insulin-producing β cells are attached to a matrix.

To establish a *prima facie* case of obviousness, the prior art reference (or references when combined) must teach or suggest all the claim limitations. *In re Vaeck*, 947 F.2d 488, 20USPQ2d 1438 (Fed. Cir. 1991); MPEP §2143.

Neither Cherksey or Jorgensen mention insulin-producing β cells or suggest a composition comprising insulin-producing β cells and RPE cells. Thus, the cited references do not support *prima facie* obviousness.

Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejections under 35 U.S.C. §103.

CONCLUSION

Applicants believe that all issues raised in the Office Action have been properly addressed in this response. Accordingly, reconsideration and allowance of the pending claims is respectfully requested. If the Examiner feels that a telephone interview would serve to facilitate resolution of any outstanding issues, the Examiner is encouraged to contact Applicants' representative at the telephone number below.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, Applicants petition for any required relief including extensions of time and authorize the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to Deposit Account No. 03-1952 referencing docket no. 311772000500. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

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Respectfully submitted,

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